

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte QI JIA, TIMOTHY C. NICHOLS,
ERIC E. RHODEN and SCOTT WAITE

Appeal 2007-4517
Application 10/091,362
Technology Center 1600

Decided: December 14, 2007

Before DONALD E. ADAMS, LORA M. GREEN, and DEMETRA J.
MILLS, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1, 4, 7, 22, 24-27, and 32-34. We have jurisdiction under 35 U.S.C. § 6(b). Claims 1 and 24 are representative of the claims on appeal, and read as follows:

1. A method for inhibiting the cyclooxygenase enzyme COX-2 comprising administering to a host in need thereof a composition comprising 10% to 100% of a mixture of Free-B-Ring flavonoids; wherein said composition is isolated from a plant selected from the Labiatae family, the *Scutellaria* genus and the *Scutellaria baicalensis* species.

24. A method for inhibiting the cyclooxygenase enzyme COX-2 comprising administering to a host in need thereof a composition comprised of 10% to 100% of a Free-B-ring flavonoid; wherein said Free-B-Ring flavonoid is selected from the group consisting of baicalein, 5,6-dihydroxy-7-methoxyflavone, 7,8-dihydroxyflavone and baicalin, wherein said composition is isolated from a plant selected from the Labiatae family, the *Scutellaria* genus and the *Scutellaria baicalensis* species.

The Examiner relies on the following references:

Newmark ('995)	US 6,264,995 B1	Jul. 24, 2001
Xinxian	US 6,290,995 B1	Sep. 18, 2001
Kuhrts	US 6,475,530 B1	Nov. 05, 2002
Newmark ('346)	US 6,391,346 B1	May 21, 2002
Newmark ('416)	US 6,387,416 B1	May. 14, 2002

Chen et al. (Chen) "Wogonin, baicalin, and baicalein inhibition of inducible nitric oxide synthase and cyclooxygenase- 2 gene expressions induced by nitric oxide synthase inhibitors and lipopolysaccharide," *Biochemical Phar.*, Vol. 61, pp. 1417-1427 (2001).

Chi et al. (Chi) "Effect of wogonin, a plant flavone from scutellaria radix, on the suppression of cyclooxygenase-2 and the induction of inducible nitric oxide synthase in lipopolysaccharide-treated RAW 264.7 cells," *Biochemical Phar.*, Vol. 61, pp.1195-1203 (2001).

We affirm.

DISCUSSION

For all rejections, Appellants group the claims into two groups: Group I comprising claims 1, 4, 7, 22, 32, and 33, with claim 1 representative; and Group II comprising claims 24-27 and 34, with claim 24 representative (Br. 5).

Claims 1, 4, 7, 24-26, and 32-34 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Chi or Chen.

According to the Examiner, the references “each teach that an extract from *Scutellaria baicalensis* is administered to a patient to inhibit or suppress COX-2.” (Answer 4.)

In order for a prior art reference to serve as an anticipatory reference; it must disclose every limitation of the claimed invention, either explicitly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

With respect to Chi, Appellants argue as to Group I, that the reference “does not disclose or suggest a composition of matter comprised of a *mixture* of free-B-ring flavonoids, but rather discloses the purported effect of one free-B-ring flavonoid, wogonin on COX-2 inhibition.” (Br. 10.)

We agree. Chi discloses that wogonin inhibits COX-2 activity directly (abstract), but does not discuss using a mixture of free-B-ring flavonoids. Thus, as Chi does not teach each and every limitation of claim 1, we are compelled to reverse the rejection as to claims 1, 4, 7, 22, 32, and 33.

As to the rejection of the Group II claims over Chi, Appellants argue that claim 24 “is drawn to a method for inhibiting the COX-2 enzyme by administering a composition comprised of 10% to 100% of a single free-B-

ring flavonoid, wherein said free-B-ring flavonoid is selected from the group consisting of baicalein, 5,6-dihydroxy-7-methoxyflavone, 7,8-dihydroxyflavone and baicalin.” (Br. 10.) Appellants assert that claim 24 does not include the free-B-ring flavonoid wogonin, and thus Chi cannot anticipate claim 24 (*id.*). We agree, and are again compelled to reverse the rejection as to claims 24-26 and 34.

With respect to Chen, Appellants argue as to Group I that Chen does not teach or suggest a composition comprised of 10% to 100% of a mixture of free-B-ring flavonoids, and in fact “teaches away from the use of compositions comprised of mixtures of flavonoids for the inhibition of COX-2 in that Chen *et al.* actually reports that no direct enzyme inhibition by any of the free-B-ring flavonoids was found.” (Br. 11.)

Chen teaches purifying the free-B-ring flavonoids baicalin, baicalein, and wogonin to a purity of 99.5 (Chen, p. 1418, second column), and uses the purified compounds in their studies. Thus, we agree with Appellants that Chen does not teach using a composition comprising 10% to 100% of a mixture of Free-B-Ring flavonoids, and we are compelled to reverse the rejection as to claims 1, 4, 7, 32, and 33.

As to the rejection of the Group II claims over Chen, Appellants argue that “claim 24 does not include the free-B-ring flavonoid wogonin and the Chen *et al.* reference expressly provides that baicalein and baicalin do not inhibit the COX-2 enzyme.” (Br. 11.)

The Group II claims, however, stand on a different footing. Chen looks at the ability of the free-B-ring flavonoids baicalin, baicalein, and wogonin to inhibit COX-2 activity in RAW 254.7 cells (Chen, p. 1419, paragraph bridging the first and second columns). PGE₂ is assayed for as a

measure of COX-2 enzyme activity (*id.*). Chen specifically teaches that “LPS-induced PGE₂ production was not inhibited by baicalin or baicalein except at 40μM, the highest concentration examined.” (Chen, p. 1420, second column.) Thus, although baicalin or baicalein are not potent inhibitors of COX-2, they did inhibit the enzyme at a concentration of 40μM. As claim 24 does not specify a concentration of the free-B-ring flavonoid, Chen reads on the method of claim 24. Thus, the rejection is affirmed as to claim 24, and claims 25-26 and 34 fall with claim 24.

Claims 1, 4, 7, 24-26, and 32-34 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Xinxian, Newmark '995, Newmark '346, Newmark '416, or Kuhlerts.

According to the Examiner, the references “each teach that an extract from *Scutellaria baicalensis* is administered to a patient to inhibit COX-2 or treat cancer which is also regulated by COX-2.” (Answer 4.)

With respect to Xinxian, Appellants argue as to Group I, that Xinxian does not teach or suggest an active mixture of free-B-ring flavonoids (Br. 14.) We agree, and the rejection is reversed as to claims 1, 4, 7, 32, and 33.

As to the rejection of the Group II claims over Xinxian, Appellants argue that although Xinxian teaches the effectiveness of baicalin in the treatment of gastric cancer, Xinxian “does not teach or suggest that the free-B-ring flavonoid, baicalin, isolated from *Scutellaria baicalensis* inhibits COX-2 activity.” (Br. 14.)

Xinxian teaches that a combination of berberine and baicalin suppressed the growth of gastric cancer cells (col. 6, Example 6). Xinxian also teaches that the combination inhibited the growth of tumor cells (col. 8,

Example 8), and also had an inhibitory effect on lung cancer (col. 8, Example 9).

As noted in the Specification:

In addition to their use as anti-inflammatory agents, another potential role for COX inhibitors is in the treatment of cancer. Over expression of COX-2 has been demonstrated in various human malignancies and inhibitors of COX-2 have been shown to be efficacious in the treatment of animals with skin, breast and bladder tumors. While the mechanism of action is not completely defined, the over expression of COX-2 has been shown to inhibit apoptosis and increase the invasiveness of tumorigenic cell types. It is possible that enhanced production of prostaglandins resulting from the over expression of COX-2 promotes cellular proliferation and consequently, increases angiogenesis.

(Specification 2-3 (references omitted).)

Thus, Xinxian teaches the administration of the free-B-ring baicalin to treat cancers such as gastric and lung cancer, and to suppress tumor growth. As the Specification also teaches the treatment of cancers, the composition of the invention and the composition of Xinxian would be administered to the same populations. Inherent anticipation does not require intent or recognition that a prior art process achieve a result which is claimed—in this case, inhibition of COX-2. “Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art.” *MEHL/Biophile*, 192 F.3d at 1365, 52 USPQ2d at 1305-06.

Thus, Xinxian anticipates the method of claim 24, and claims 25-26 and 34 fall with claim 24.

With respect to Newmark '995, Appellants argue that “even though the Newmark *et al.* composition likely contains free-B-ring flavonoids, there is no disclosure or suggestion that these compounds are COX-2 inhibitors.” (Br. 15.) Appellants argue further that the maximum percentage of baicalin in Newmark’s composition is 1.3%, and thus Newmark '995 cannot anticipate the claims, as the claims require 10% to 100% of a Free-B-ring flavonoid (*id.* at 16).

As the Examiner has not provided evidence or arguments to refute Appellants’ calculations as to the maximum percentage of baicalin in the composition of Newmark '995, we are compelled to reverse the rejection under § 102(e) over Newmark '995.

With respect to Newmark '416, Appellants reiterate their arguments as to Newmark '995 (Br. 16). For the reasons set forth above with respect to Newmark '995, we are also compelled to reverse the rejection under § 102(e) over Newmark '416.

With respect to Newmark '346, Appellants argue again that the reference “does not teach or suggest the use of free-B-ring flavonoids or mixtures thereof as COX-2 inhibitors.” (Br. 17.) Moreover, Appellants assert, the maximum amount of free-B-ring flavonoids in the composition is 6-9% by weight (*id.*). According to Appellants, “the claims of the instant invention provide that the free-B-ring flavonoid or mixture thereof is present in an amount greater than 10%. Therefore, based on the above reasoning, this patent does not anticipate the claims of this invention.” (*Id.*)

Again, as the Examiner has not provided evidence or arguments to refute Appellants’ calculations, we are compelled to reverse the rejection under § 102(e) over Newmark '346.

With respect to Kuhrts, Appellants argue that the plant *Scutellaria baicalensis* was referred to as the COX-2 inhibitor, but that there is no further description as to the material or extract being used, nor to the amounts or dosage (Br. 17). According to Appellants, “there have been more than 58 compounds isolated from various parts of *Scutellaria baicalensis*. These compounds include alkaloids, benzyl alcohol glycosides, lignans, benzopyranones, amino acids, phytosterols, monosugars, flavones, and flavanones. The Kuhrts patent provides no examples to substantiate the claim of a COX inhibitor from *Scutellaria baicalensis*.” (*Id.*) Appellants assert that Kuhrts does not “teach or suggest the use of free-B-ring flavonoids or mixtures thereof as COX-2 inhibitors.” (*Id.*) We agree that Kuhrts does not teach the amounts of *Scutellaria baicalensis* to be used as the COX-2 inhibitor, and we are compelled to reverse the rejection.

Claims 1, 4, 7, 22, 24-27, and 32-34 stand rejected under 35 U.S.C. § 103(a) as being obvious over Chi, Chen, Xinxian, Newmark '995, Newmark '346, Newmark '416, or Kuhrts.

The references are relied upon as in the rejections made under § 102 (Answer 5). According to the Examiner:

The amounts used are simply the choice of the artisan to use in an effort to optimize the desired results. The range of 2.0 to 200 mg/kg of body weight is a very broad range and while the references may not use the same measurements of the amount of the extract as appellants do, it is clearly within the purview of the skilled artisan to use such broad ranges since such broad ranges would clearly encompasses so many different amounts that one could use in administering this well known plant extract for a well known use.

(*Id.*)

“In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant.” *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted). In order to determine whether a prima facie case of obviousness has been established, we consider the factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1996): (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present.

With respect to the obviousness rejection over Chi, Appellants basically reiterate their arguments as to the rejection under § 102(a) over Chi (Br. 21). For the reasons set forth above with respect to that rejection, we are also compelled to reverse the rejection under § 103(a) over Chi. Specifically, the Examiner’s obviousness rejection is based on optimization of amounts of the free-B-ring flavonoid, and Chi does not teach using a mixture of free-B-ring flavonoids, and also does not disclose a method for inhibiting the COX-2 enzyme by administering a composition comprised of 10% to 100% of a single free-B-ring flavonoid, wherein said free-B-ring flavonoid is selected from the group consisting of baicalein, 5,6-dihydroxy-7-methoxyflavone, 7,8-dihydroxyflavone and baicalin.

With respect to the obviousness rejection over Chen, Appellants again reiterate their arguments as to the rejection under § 102(a) over Chen (Br. 21-22). As Chen does not disclose using a mixture of free-B-ring flavonoids, and as the Examiner fails to provide argument or evidence as to

why the use of such a mixture would have been obvious over the teachings of Chen, we are compelled to reverse the obviousness rejection as to the claims in Group I, *i.e.*, claims 1, 4, 7, 22, 32, and 33.

As we have affirmed the rejection under § 102(a) over the claims of Group II, *i.e.*, claims 24-27 and 34, and as anticipation is the epitome of obviousness, *In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002), we affirm the obviousness rejection over Chen as to Group II.

With respect to the obviousness rejection over Xinxian, Appellants again reiterate their arguments as to the rejection under § 102(a) over Xinxian (Br. 23). As Xinxian does not disclose using a mixture of free-B-ring flavonoids, and as the Examiner fails to provide argument or evidence as to why the use of such a mixture would have been obvious over the teachings of Chen, we are compelled to reverse the obviousness rejection as to the claims in Group I, *i.e.*, claims 1, 4, 7, 22, 32, and 33.

As we have affirmed the rejection under § 102(a) over the claims of Group II, *i.e.*, claims 24-27 and 34, and as anticipation is the epitome of obviousness, we affirm the obviousness rejection over Xinxian as to Group II.

With respect to the obviousness rejection over Newark '995, Appellants argue that the '995 patent "does not teach or suggest the use of free-B-ring flavonoids or mixtures thereof as COX-2 inhibitors. The present invention, on the other hand, discloses and claims a specific class of compounds, free-B-ring flavonoids, as having COX-2 inhibitory activity." (Br. 24.) Thus, according to Appellants, "even though the . . . composition likely contains free-B-ring flavonoids, there is no disclosure or discussion that these compounds are COX-2 inhibitors." (*Id.*)

Appellants argue further

that there are many advantages to isolating and identifying specific biologically active compounds from a composition of matter that could contain literally thousands of compounds. Once identified a class of compounds can be purified and concentrated to provide a more effective biological agent. Additionally, the compounds can be chemically modified to provide a composition of matter that is more active and or less toxic. Finally, once isolated and identified a specific compound or class of compounds can be studied to determine the exact biological activity and mode of action, thus enabling more specific targeting of the compound or class of compounds to treatment of particular diseases or conditions. Contrary to the Examiner's assertion that optimization of factors such as concentration is standard practice, unless one knows what specific compound or class of compounds is exhibiting the desired activity, one cannot possibly optimize the concentration of that compound or class of compounds.

(*Id.*)

Appellants' arguments are not convincing. First, as Appellants have not argued the claims separately, we focus our analysis on claim 1, and claims 4, 7, 22, 24-27, and 32-34 fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

Newark '995 teaches an herbal composition which inhibits the COX-2 enzyme for reducing bone and joint inflammation (col. 7, ll. 42-45). One of the components of the composition is a root extract of *Scutellaria baicalensis* (Col. 12, Table).

As noted by the Specification, the "Chinese medicinal plant, *Scutellaria baicalensis* contains significant amounts of Free-B-Ring flavonoids, including baicalein, baicalin, wogonin and baicalenoside." (Specification 5.) Thus, the composition of Newark '955 would also contain

those free-B-ring flavonoids, which flavonoids are inherently COX-2 inhibitors. Moreover, although Newark '955 does not specifically teach that the free-B-ring flavonoids have COX-2 activity, the reference does teach that composition containing the root extract of *Scutellaria baicalensis* is a COX-2 inhibitor. Thus, it would have been obvious to the ordinary artisan to optimize the amount of *Scutellaria baicalensis* to optimize the ability of the composition to inhibit COX-2. See *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980) (“[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art.” (citations omitted)). As noted by the Examiner, a composition containing 10-100% of a mixture of free-B-ring flavonoids is a very broad range.

We have considered Appellants arguments as to the many advantages to isolating and identifying specific biologically active compounds from a composition of matter that could contain literally thousands of compounds. However, claim 1 does not exclude the use of the extract. Thus, we conclude that the method of claim 1 is obvious over the teachings of Newark '955. As claims 4, 7, 22, 24-27, and 32-34, fall with claim 1, the rejection is affirmed as to all of the rejected claims.

As to the obviousness rejection over Newark '416 and Newark '346, Appellants basically reiterate their arguments as to Newark '955 (Br. 24-25). Thus, the obviousness rejections of claims 1, 4, 7, 22, 24-27, and 32-34 over those two references is affirmed for the reasons set forth above with respect to the obviousness rejection over Newark '955.

With respect to the obviousness rejection over Kuhrt, Appellants argue that

Scutellaria baicalensis was referred to in the patent as a COX-2 inhibitor. There is no further description, however, of the material or extract of *Scutellaria baicalensis* being used. Nor is there any reference to amounts or dosage. “*Scutellaria baicalensis*” is the Latin name of a specific species of plant. As is commonly known that different parts of a plant contain totally different types of compounds in different concentrations. To date, there have been more than 58 compounds isolated from various parts of *Scutellaria baicalensis*. The Kuhrts patent does not teach or suggest the use of free-B-ring flavonoids or mixtures thereof as COX-2 inhibitors. Therefore, for the reasons discussed above, Applicant maintains that the Kuhrts patent does not render the present method obvious.

(Br. 25.)

Appellants’ arguments are not convincing. First, as Appellants have not argued the claims separately, we focus our analysis on claim 1, and claims 4, 7, 22, 24-27, and 32-34 fall with claim 1.

Kuhrts teaches a composition for weight loss containing a COX-2 inhibitor, such as *Scutellaria baicalensis* (Kuhrts, col. 6, ll. 2336). As noted above, *Scutellaria baicalensis* contains significant amounts of free-B-ring flavonoids, which are COX-2 inhibitors. As Kuhrts teaches using the *Scutellaria baicalensis* as a COX-2 inhibitor, it would have been obvious to the ordinary artisan to optimize the amount of *Scutellaria baicalensis* to optimize the ability of the composition to inhibit COX-2. As noted by the Examiner, a composition containing 10-100% of a mixture of free-B-ring flavonoids is a very broad range.

Thus, we conclude that the method of claim 1 is obvious over the teachings of Kuhrts. As claims 4, 7, 22, 24-27, and 32-34 fall with claim 1, the rejection is affirmed as to all of the rejected claims.

CONCLUSION

In summary, we:

Reverse the rejections under 35 U.S.C. § 102(a) and § 103(a) over Chi.

Affirm the rejection of claims 24-26 and 34 under 35 U.S.C. § 102(a) and § 103(a) over Chen and Xinxian, but reverse as to the remainder of the claims.

Reverse the rejections of claims 1, 4, 7, 24-26, 32, and 34 under 35 U.S.C. § 102(e) over Newmark '995, Newmark '346, Newmark '416, and Kuhrts, but affirm the rejections of claims 1, 4, 7, 22, 24-27, and 32-34 under 35 U.S.C. § 103(a) as to those references.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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